RESPONSE UNDER 37 C.F.R. §1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1631

PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Jonathan Miller, et al.	**Examiner:**	Michael L. Borin
Serial No.:	09/730,214	**Art Unit:**	1631
Filed:	December 5, 2000	**Docket:**	13993
For:	METHOD AND SYSTEM FOR DESIGNING PROTEINS AND PROTEIN BACKBONE CONFIGURATIONS	**Dated:**	March 31, 2003

Commissioner for Patents
Washington, D.C. 20231

RESPONSE UNDER 37 C.F.R. §1.116

Sir:

In response to the Official Action dated September 23, 2002, and in accordance with the provisions of 37 C.F.R. §1.116, Applicants respectfully submit the following amendment in connection with a concurrently filed Request for Continued Examination pursuant to 37 C.F.R. §1.114 in the above-identified case.

CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231 on March 31, 2003.

Dated: March 31, 2003

Michelle Mustafa

REMARKS

The Examiner has rejected claims 22-40 under 35 U.S.C. §101 and §112, first paragraph as allegedly lacking utility. Applicants respectfully submit that the invention is useful and enabled in full satisfaction of 35 U.S.C. §101 and §112, first paragraph. The specification discloses a specific and substantial utility and permits the skilled artisan to immediately appreciate its usefulness. *Brenner v. Manson* 383 U.S. 519, 148 U.S.P.Q. 689 (1966).

The Examiner asserts that the invention does not provide an "adequate nexus between the evidence of record and the asserted properties of the claimed subject matter". Official Action, September 23, 2003, p. 3. The invention is directed to a method of designing proteins. The Examiner contends that the utility requirements are ignored by Applicants because further research is required to identify or confirm a 'real world' context of use. Id.

The Examiner appears to confuse the claimed invention as relating to a product, i.e. a protein or a product produced by the claimed process. However, it is unquestionable that the claimed invention relates to a method of designing proteins using a series of delineated steps (See, claim 22). One result of the process is the formation of a desirable protein configuration, such as is discussed in relation to Figure 5, wherein the specification specifically teaches and illustrates the synthesis of a structure 150, which resembles the natural zinc finger protein (See, Page 11, Lines 9-12 and Figure 5, Panel D, for example). Thus, not only is the claimed method detailed by the instant specification, but a recognized product is capable of being produced thereby.

It is the claimed invention that is the focus of the utility requirement. See MPEP 2107.02. Inasmuch as the Applicants have established utility for the method embodied in claim 22, the sole independent claim at issue, the dependent claims 23-40 should be treated as being sufficient under 35 U.S.C. §101.

Moreover, multiple utilities of the claimed invention are offered by Applicants, including the ability to design novel small protein structures for use as research tools to address the so-called "protein folding problem". An Applicant need only make one credible assertion of specific utility for the claimed invention to satisfy 35 U.S.C. §101 and 35 U.S.C. §112; additional statements of utility, even if not "credible", do not render the claimed invention lacking in utility. See e.g. *Raytheon v. Roper*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983) *cert. denied* 469 U.S. 835 (1984).

Notably, the Examiner has failed to satisfy the initial burden to establish a prima facie showing that the claimed invention lacks utility. The Examiner relies on Shakhnovitch ((1998) Folding and Design 3:R45-R58 (hereinafter "Shakhnovitch")) to assert that the design of new proteins has enjoyed limited success in that polypeptides fold into disordered configurations. Applicants respectfully submit that the success or failure to design a new protein is simply not the subject of the claimed invention. On this basis alone, rejection under 35 U.S.C. §101 is improper and should be withdrawn. See *In re Oetiker* 977 F.2d 1443, 1445, 24 U.S.P.Q. 2d 1443, 1444 (Fed. Cir. 1992).

Furthermore, Shakhnovitch teaches at R45 and R55 that reliable approaches to protein design will justify the effort to address the protein folding problem which is specifically described by the specification as a useful aspect of claimed invention. (See specification, Page 4, Lines 29-31) Thus, given the identification of a specific protein backbone structure obtained by the claimed method and the disclosure of a use relating to solving the protein-folding problem, it is unquestionable that the present invention fully satisfies the requirements of 35 U.S.C. §101 and a rejection based thereon was reversible error. The Examiner is therefore respectfully requested to reconsider and withdraw the rejection of claims 22-40 under 35 U.S.C. §101.

Moreover, the specification provides a detailed roadmap enabling the skilled artisan to perform a method to design novel proteins. See Page 6, Line 30-Page 12, Line 30. Assuming, pro arguendo, the Examiner established a prima facie case for lack of utility, Applicants have clearly rebutted such presumption and the Examiner must therefore withdraw the corresponding rejection imposed under 35 U.S.C. §112, first paragraph. See MPEP 2107, II. Accordingly, the rejections of claims 22-40 under 35 U.S.C. §101 and §112, first paragraph are overcome and withdrawal thereof is respectfully requested.

Claims 22-40 have been rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Balaji et al. in view of Cohen et al. or Lee et al. Applicants submit that the cited references fail to teach or suggest the claimed invention. The Examiner alleges that Balaji et al. teach a method for designing peptide mimetics based on a method for predicting a stable tertiary structure of a peptide comprising generating protein backbone configurations using dihedral angles phi and psi, analyzing and plotting the phi, psi angle distribution and determining the state with minimum energy. The Examiner admits that the reference fails to teach the elimination of self-intersecting configurations. Applicants submit that Balaji et al. merely attempt to identify the folded state of particular peptide sequences. Balaji et al. require molecular mechanics to find possible low-energy configurations for a known specific sequence. Notably, Balaji et al. do not suggest, no less motivate the skilled artisan to employ the claimed method design new protein structures. It is therefore respectfully submitted that the rejection is improper because there is nothing in Balaji et al. to suggest the claimed method in the first instance or that the claimed invention is obvious to one or ordinary skill in the art in view of the teachings therein. As the court states in W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-313, (Fed. Cir. 1983), cert denied, 469 U.S. 851 (1984):

> To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, one falls victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher.

Thus, it is improper to sustain a §103 rejection under these circumstances. Id.

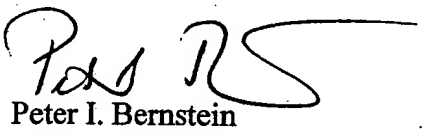
As indicated hereinabove, Balaji et al. do not provide any teaching that the process described therein would produce proteins inasmuch as the reference admittedly fails to address a critical feature of the claimed invention, namely the elimination of self-intersecting configurations, and without such teaching, it is improper to imbue the skilled artisan with any such knowledge. It is respectfully submitted that the Examiner is engaging in a hindsight reconstruction of the art which is not the proper basis to sustain an obviousness rejection. Furthermore, the Balaji et al. method is inoperable unless the "threading" algorithm is employed. Notably, the claimed invention does not require a threading algorithm. Moreover, the claimed method does not require any form of molecular mechanics as detailed in the cited references.

The teaching of the secondary references Cohen et al. or Lee et al. fail to ameliorate the deficiencies of the primary reference. The Examiner alleges that Cohen et al. teach that estimations of hydrophobicity and hydrophilicity are helpful in the verification of 3D models determined from angle or energy calculations. The Examiner also alleges that Lee et al. teach a method for determining peptide 3D structure. Applicants submit that neither Cohen et al. or Lee et al. identify new protein structures. Cohen et al. utilize a threading algorithm, that is they examine a particular sequence on several known protein structures to predict the folding of that sequence. Lee et al. examine the energy of a specific sequence on a particular known protein structure, with fixed backbone, allowing only for different conformations of the side chains. None of the cited references suggest, no less motivate the skilled artisan to generate new

protein structures, as claimed. Accordingly, the rejection of claims 22-40 under 35 U.S.C. §103(a) is overcome and withdrawal thereof is respectfully requested.

Thus, in view of the foregoing remarks, Applicants respectfully submit that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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